REMARKS/ARGUMENTS

Claims 1-8 are pending in the present application. Claim 1 is slightly amended for better format. No new matter is added. Reconsideration of the present application is respectfully solicited in view of the following remarks.

Claims 1-8 stand rejected under 35 U.S.C. § 103 as unpatentable over Dolitzky et al. (WO 02/45658) in view of Rameshchandra et al. (WO03/050074). [1] Applicants respectfully traverse.

Independent claim 1 recites a process for preparing an acid addition salt of venlafaxine which comprises, among other things, **(a) converting a venlafaxine precursor to venlafaxine in an aqueous solution; (b) extracting venlafaxine from the aqueous solution with a water-immiscible organic solvent to obtain an organic venlafaxine solution; and (c) reacting the organic venlafaxine solution with an acid to prepare the acid addition salt of venlafaxine.**

Based on the above bold language, claim 1 clearly reflects that the acid addition salt of venlafaxine is prepared by directly reacting a solution of venlafaxine with an acid in an organic solvent, which solvent is previously used for extracting venlafaxine from an aqueous reaction solution. In other words, according to claim 1, no step of isolating a solid or residue venlafaxine base from an organic phase, which is previously obtained during the extracting step, is conducted. The same water immiscible organic solvent used in the extracting step is also present in the subsequent step of reacting venlafaxine base with an acid.

Nevertheless, the Examiner ignores the above-discussed limitations of claim 1 in the Office Action and therefore fails to identify any disclosure in Dolitzky or Rameschandra that discloses these limitations. Indeed, neither Dolitzky nor Rameschandra discloses such limitations. These two references actually teach away from the method of claim 1.

Specifically, unlike the present invention, Dolitzky discloses that that prior to the reaction with an acid to make a venlafaxine salt, solid venlafaxine base should be first isolated from an organic solution by evaporating an organic solvent that is contained therein and previously used for extracting the venlafaxine based from an aqueous reaction solution. *See*, for example, page 6, lines 12-24, Examples 1, 2, and 13. Although the ultimately produced venlafaxine salt of Dolitzky has sufficient purity, one would not conclude that the step of isolating venlafaxine base from the extracting organic phase should be omitted. On the

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[1] Dolitzkyl is identified in the Office Action as WO 00/45658, which Applicants believe should be WO 02/45658 listed in Applicants' previously submitted IDS. Similarly, Rameshchandra is identified in the Office Action as WO 02/050074, which Applicants believe should be WO 03/050074 listed in Applicants' previously submitted IDS. Neither of the references as literally identified by the Office Action appears to be relevant to the present application. Should Applicants' assumption herein for facilitating the prosecution is incorrect, Applicants respectfully request that these two references be correctly identified.

contrary, one would reasonably conclude that the isolation step is essential and cannot be omitted to obtain a final acid salt of venlafaxine product with a satisfactory purity. (The HPLC purity of the venlafaxine hydrochloride obtained in each of Examples 2-3 of the present application, which are embodiments of the present invention, is 99.65 area%)

Similarly, the other reference Rameschandra also discloses that pure solid venlafaxine base should be used for making venlafaxine hydrochloride. *See* page 8, lines 1-2. Nowhere does Rameschandra teach reacting a venlafaxine solution, which contains a water immiscible organic solvent that is previously used to extract venlafaxine from the reaction solution, with an acid to prepare the acid addition salt of venlafaxine, as described in claim 1 of the present application. Moreover, because Rameschandra discloses that pure solid venlafaxine base should be used, which is expected to have a high purity, one would not expect success of reacting a venlafaxine base, which is not isolated from an organic solvent previously used for extracting venlafaxine from a reaction solution, with an acid. In other words, Rameschandra teaches away from the method of claim 1.

Therefore, combining Dolitzky and Rameschandra, as proposed by the Examiner, would not have arrived at the method of claim 1 or any of its dependent claims 2-7 of the present application. For at least this reason, claims 1-8 are not obvious under 35 U.S.C. § 103 over Dolitzky in view of Rameshchandra.

Additionally, the Examiner appears to acknowledge that the primary reference Dolitzky fails to disclose reacting venlafaxine solution with an acid to prepare the acid addition salt of venlafaxine in the presence of a water-immiscible organic solvent. Indeed, Dolitzky discloses the use of water miscible solvent acetone or isopropyl alcohol during the converting reaction of venlafaxine to venlafaxine hydrochloride. *See* page 4, lines 1-4 and Figure 10 of Dolitzky. Therefore, the Examiner resorts to the second reference Rameshchandra to remedy the deficiency of Dolitzky. Nevertheless, the Examiner fails to realize that, according to claim 1 of the present application, the water immiscible solvent present during the reaction of venlafaxine solution with an acid is not newly added but comes from the previous step of extracting venlafaxine base. Rameshandra only mentions the possibility of **adding** a water immiscible solvent **during the reaction of a pure solid venlafaxine with an acid.** Rameshandra by no means teaches that the water immiscible solvent used during the reaction of venlafaxine base with an acid derives from the previous step of extracting venlafaxine base from an aqueous reaction solution. Therefore, Rameshchandra cannot properly remedy the deficiency of Dolitzky.

Based on the foregoing, claims 1-8 are not obvious over Dolitzky and Rameshandra under 35 U.S.C. § 103. It is respectfully requested that the rejection of claims 1-8 be withdrawn.

It is believed that the present application is in a condition for allowance, early notice of which is earnestly solicited.

If any fees or charges are required at this time, they may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

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